Remarks

The Office action mailed November 7, 2003, has been reviewed and carefully considered. Claims 29, 46 and 47 have been amended for purposes of further clarification. The amendments to claims 29, 46 and 47 find support in the application, for example, at page 10, lines 22-26. Claims 30, 48 and 55 have been amended to define the moiety "Z." The amendments to claims 30, 48 and 55 find support in the application, for example, at page 3, line 9. Claims 32, 35, 50, 53, 57 and 60 have been amended for purposes of clarification. New claims 62-64 have been added. Support for claims 62-64 is found in the application, for example, in originally filed claims 32, 50 and 57, respectively. Entry of these amendments is respectfully requested.

Claims 29-38 and 46-61 stand rejected under 35 U.S.C. §112, second paragraph, due to the examiner's concerns with the R_5, R_6, and Z moieties. Although the rejection states that it is applied to all of the pending claims, claims 30-36, 38, and 48-61 do not recite any of the language objected to by the examiner, and thus the rejection cannot apply to claims 30-36, 38, and 48-61. With respect to claims 29, 37, 46 and 47, it is submitted that the 35 U.S.C. §112, second paragraph, rejections have been obviated by the present amendments.

Claims 29-38 and 46-61 also stand rejected under the so-called judicially-created doctrine of an improper Markush group. Applicants first point out that the existence of such a "doctrine" was repudiated by the Court of Customs and Patent Appeals (CCPA) which is the predecessor to the Court of Appeals for the Federal Circuit. *See In re Harnisch*, 206 USPQ 300, 303 (CCPA 1980) ("there is no Markush doctrine") (attached as Exhibit 1). MPEP §803.02, which was cited by the examiner in the Office action mailed May 13, 2003 (paper no. 9), discusses Markush practice, but in the context of a restriction requirement, not as the basis by itself for a claim rejection. It is instructive to realize that none of the four cases cited in MPEP §803.02 (*In re Weber*, *In re Haas, In re Harnisch*, *Ex parte Hozumi*) (attached as Exhibits 2, 3, 1 and 4, respectively) or *In re Jones*, 74 USPQ 149 (CCPA 1947) (cited by the examiner and attached as Exhibit 5) upheld a Markush group rejection. Thus, an objection to Markush language can be the basis for a restriction requirement, but a claim rejection based on such objections is tenuous at best. A restriction requirement has already been made by the examiner as set forth in the Office action mailed February 26, 2003 (paper no. 7). In view of this restriction requirement, a claim rejection based on the Markush form of the claims is improper.

In addition, contrary to the examiner's assertion, unity of invention is present since the claimed compounds "(1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility." *See* MPEP §803.02. All the compounds share a common utility - anti-integrase inhibitors. All the compounds share a substantial structural feature - thiazepine or thazepine analog structure - that is important to their utility as anti-integrase inhibitors. The facts of the present application are similar to those in *In re Harnisch*, *Ex parte Hozumi* and *In re Jones*, all of which reversed an improper Markush rejection. In *In re Harnisch*, all the claimed compounds were dyes and coumarin compounds that were defined by a generic formula. In *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. Int. 1987), all the compounds exhibited antimycotic activity and were phosphoric acid diesters that were defined by a generic formula. In *In re Jones*, all the compounds were insecticides or fungicides and were derivatives of tetrahydronaphthalene that were defined by a generic formula. It is apparent from these cases that the common utility and structure requirement has been applied very broadly. The court in *In re Harnisch*, 206 USPQ at 305 also noted "that in any Markush group the compounds will differ from each other in certain respects." (quoting *In re Jones*, 74 USPQ at 151). Thus, simply because the presently recited formulae cover various compounds does not justify an improper Markush rejection.

At this stage of prosecution, the examiner must follow the guidelines outlined in MPEP §803.02. According to this section of the MPEP, "should no prior art be found that anticipates or renders obvious the elected species, the search of Markush-type claim will be extended." No prior art has been cited by the examiner that anticipates or renders obvious the elected species in the present application. Moreover, it appears that the examiner has already extended the search to a certain extent beyond the elected species. Under these circumstances, it is submitted that applicants are now entitled to the generic Markush claims.

Claims 46 and 48-54 also have been rejected under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement. More specifically, the examiner asserts that "the specification fails to teach any benefit to be gained" from *in vitro* inhibition of HIV integrase. The Office action does not appear to specify whether this is a rejection based on an alleged failure to enable one to make the claimed invention or use the claimed invention. In any event, it is submitted that this rejection must be reconsidered and withdrawn. The specification contains a detailed description of an *in vitro* integrase assay (see Example 5 on page 23) and a multitude of

examples of compounds that exhibited anti-integrase activity as tested in an integrase assay (see Table 1 on page 26). Thus, the specification clearly teaches how to perform an *in vitro* assay that determines whether a particular compound inhibits HIV integrase *in vitro*. The benefit of such *in vitro* testing methods also is described in the specification, and would be readily apparent to a skilled artisan.

The specification states that the disclosed methods include "methods of screening for an anti-HIV integrase drug, by providing an assay of HIV integrase inhibition, and using the assay to screen for drugs that are analogs or derivatives of any of the compounds, and which inhibit HIV integrase" (page 9, lines 10-13). Thus, *in vitro* testing of the presently claimed compounds for anti-HIV integrase is useful for identifying possible lead compounds for further exploration.

Moreover, it is common (if not universal) practice in searches for new drugs that the initial screening of candidate compounds is done via *in vitro* methods that are designed to identify certain pharmacological properties such as integrase inhibition. The myriad problems that would be associated with initially testing every candidate compounds are well-known (e.g., patient safety, cost, time, etc.) Such *in vitro* methods have paramount importance in the discovery of new drugs.

It is respectfully submitted that the application is now in condition for allowance. Should there be any questions regarding this application, Examiner Kifle is invited to contact the undersigned attorney at the telephone number shown below.

Respectfully submitted,

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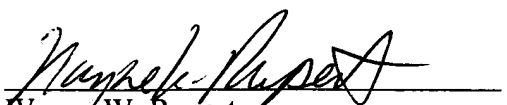
By 
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